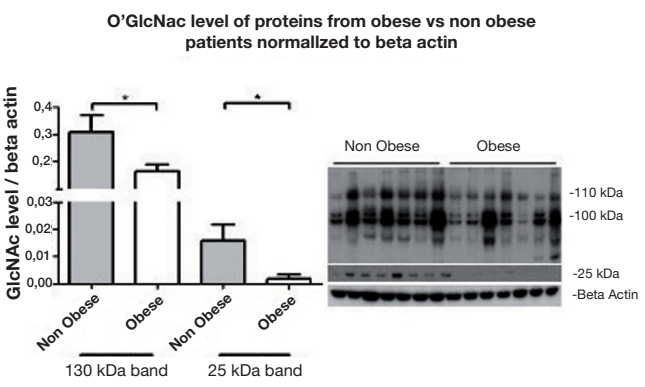
meric proteins including phosphorylation and O'GlcNacylation. Finally we explored the acute ex vivo effect of the modulation of O'GlcNac on the myofilament sensitivity to calcium. There was a significant contractile dysfunction in obese subjects compared to normal subjects, in both the force (p=0.01) and myofilaments sensitivity to calcium concerning the Fmax (p=0.03). No change in the expression of genes encoding sarcomeric proteins or enzymes involved in post-translationnal modification; nor phosphorylation modification of sarcomeric proteins like cMLC2 or cTnI in obese patients was observed. Conversely, we showed in obese patients a decreasing O'GlcNacylation of proteins of 25 kDa (p=0.007) and 130 kDa (p=0.03) which include the sarcomeric proteins MLC2 and Troponin I. Finally, we pointed out that alteration of the O'GlcNac level by Azaserin decreased the cardiac myofilaments sensitivity to calcium pCa50 (p=0.05). This study highlights before clinical and echocardiographic onset, an association between impaired contractile function, an altered sensitivity to calcium, and a decreased O'GlcNacylation of possible sarcomeric proteins in humans.



Abstract 0048 – Figure: Level of O'GlcNac of myofilaments proteins

0470

Role of Lipocalin 2 (LCN2) in cardiovascular remodeling induced by aldosterone

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Neutrophil Gelatinase Associated Lipocalin or Lipocalin 2 (LCN2) is a circulating protein, member of the lipocalin family, which binds MMP9 and modulates its stability and activity. We have recently shown that LCN2 is a primary target of aldosterone/mineralocorticoid receptor (MR) in endothelial cells, vascular smooth muscle cells and cardiomyocytes. We hypothesized that LCN2 could be a mediator of aldosterone/MR profibrotic and proinflammatory effects in the cardiovascular system. Wild type (WT) and LCN2 Knock Out (KO) mice were subjected to an uni-nephrectomy aldosterone salt challenge (NAS, 200µg/kg/day of aldo, 1% NaCl in tap water) for 4 weeks. Blood pressure (SBP) was measured by tail cuff method. Cardiovascular fibrosis and inflammation were analyzed by RT-PCR, western blot, immunohistochemistry and ELISA. There was no difference in SBP between transgenic mice compared to WT mice in basal condition. With NAS challenge, SBP was increased only in WT mice (SBP; CT 107±3, CT NAS 133±5, KO 109±3, KO NAS 115±3 mmHg). Quantification of pro collagen I N-terminal peptide (PINP) in plasma showed an increase of PINP due to NAS treatment in WT that was prevented by LCN2 inactivation (CT 83±15, CT NAS 129±10, KO 70±19, KO NAS 59±12 µg/l). In myocardium, NAS treatment increased collagen type I and perivascular fibrosis in WT whereas KO were resistant to fibrosis (Collagen Volume Fraction; CT 19±3, CT NAS 28±2, KO 20±3, KO NAS 20±3%). In aorta, collagen type I, vascular fibrosis and osteopontin were also increased by NAS in WT. These increases were prevented by LCN2 inactivation (CVF; CT 24±4, CT NAS 34±5, KO 21±2, KO NAS 28±2%). Our results show that LCN2 plays a key role in aldosterone/MR-mediated vascular fibrosis and inflammation, but not in cardiac interstitial fibrosis and vascular dysfunction. We are now analyzing 1) the specificity of aldo/MR versus other pro-fibrotic challenges (AngII, catecholamines) as well as 2) the role of inflammation in the effects mediated by Lcn2.

0253

Sympathetic overactivity: a very early manifestation of metabolic syndrome

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Sympathetic overactivity is a hallmark of metabolic syndrome (MS). Data showing sympathetic overactivity in patients with early cardiovascular and metabolic disorders, i.e., prodromal forms of MS, are lacking. Sympathetic activity was measured by microneurography (MSNA), heart rate variability (HRV), blood pressure variability (BPV) and plasma and urinary catecholamines. β_2-adrenergic receptor (β_2-AR) and the G-protein coupled receptor kinase 2 (GRK2) mRNA expression levels were tested as possible markers of sympathetic activity in blood mononuclear cells (PBMCs). 40 healthy volunteers and 16 patients with established (3 components of the MS) and 23 incomplete (two components) MS were compared. MSNA was not only increased in patients with overt MS but also among patients with incomplete MS (P<0.001). In PBMCs of patients with incomplete MS, a significant 3.4 fold increase in the β_2-AR over GRK2 mRNAs expression ratio was observed (P=0.001); this ratio correlated well with MSNA. (Funded by the Clinical Research program of the French Ministery of Health)

0426

Admission glycaemia: the crystal ball to assess prognosis value after STEMI

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Introduction: High glycaemia at admission in STEMI patients is common and associated with an increased risk of in-hospital and post-discharge death.

Aim: To evaluate the impact of admission glycaemia in the short prognosis of diabetic and non-diabetic patients admitted for STEMI and to identify independent predictors of post-ACS mortality.

Population and methods: This study included 567 patients admitted to a single coronary care unit for STEMI, between January 2004 and June 2012. Our population was divided in three groups according to the tertiles of glycaemia at admission (T1<7; T2=7-11 e T3>11 mmol/l). Rates of success after revascularisation, intrahospital mortality, and ventricular arrhythmias were collected

Results: Hyperglycaemia at admission was associated to worse cardiovascular risk profile, more severe coronary disease (more 3 vessel disease), incomplete revascularization, higher creatinine levels and more life threatening ventricular arrhythmias (VT/VF). In the predefined tertiles, in-hospital mortality was 4%, 5.2% and 14% (p<0.001). Life threatening arrhythmias were respectively 2.4%; 4% and 9% (p:0.017). In the group of patients with glycemia >11 mmol/l (224 patients), outcomes were similar between the diabetic and non diabetic patients with death rates respectively 13.8% and 13.9% (p:0.988) In a multivariate analysis, predictive factors of intrahospital mor-